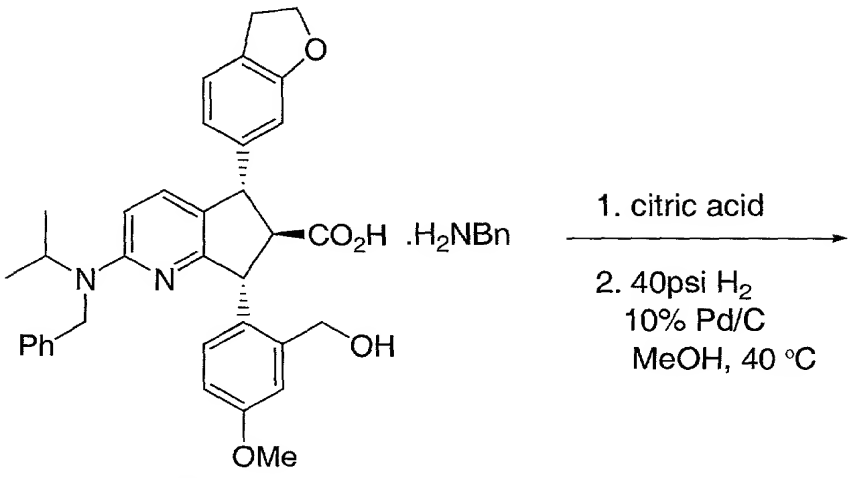
The completion of the deprotection is confirmed by HPLC (<2% t-butyl ester intermediate).

HPLC conditions: Zorbax SB-C8 4.6 x 250mm; MeCN 30-80% in 15 min; 1.50mL/min, pH=7, 10mM Trizma buffer; 30°C, UV detection at 220nm; Retention times (min): t-butyl ester intermediate (17.9), deprotection product (9.1), and trityl alcohol (12.2).

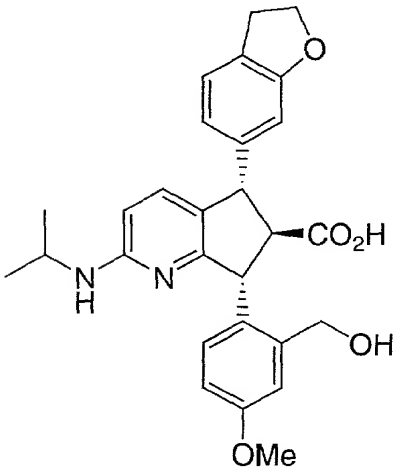
The mixture is then cooled to 0°C and neutralized with NaOH (10N, 1.16L at <25°C) until the pH of the aqueous layer is between 5 and 7. Water (500mL) is added to dissolve the precipitated inorganic salt after neutralization. About 1L of MTBE is added and the mixture is stirred for 15 minutes. The mixture is then allowed to settle for about 20 minutes and the layers are separated. The organic layer is extracted with NaOH. Assay of the organic layer indicates about 1% to 2% product loss. The combined aqueous layer is back extracted with MTBE and the back extract is then washed with 0.1N NaOH. About 1.5L of MTBE is added to the combined NaOH extracts, and then the mixture is neutralized with 2N HCl to pH of about 5 to 6. The organic layer is separated and then washed with brine. The brine washes are combined with the aqueous layer and then extracted with 1L of IPAc. The organic layer is washed with brine. The combined organic layer is concentrated to a minimum volume of about 0.4L and flushed with 1L of IPAc. The residue is diluted with isopropyl alcohol (IPAC) and treated with about 10g of Darco-KB for 2 hours. The mixture is then filtered through a Solka-Floc pad. The pad is rinsed with IPAc. Assay of the filtrate indicated the presence of 175g (77% overall yield from Michael addition) of the product as its benzylamine salt equivalent. It is concentrated to 844g and then 15mL of benzylamine and 1g of seed are added. The mixture is then stirred under nitrogen for 3 hours. The remaining benzyamine is added slowly for an hour, and then the mixture is stirred overnight at room temperature. The product is collected by filtration and the filter cake is washed with IPAc until the wash becomes almost colorless. The product is dried by sucking air through it for about 3 hours until constant weight is obtained to give 158g of the benzylamine salt **20** (97.3 A%, 70% overall yield from Michael addition). Mother liquor loss is 18g (8.0%).

EXAMPLE 13

Hydrogenolysis of benzlamine salt (20):




**20**




**21**

To a slurry of the benzylamine salt **20** (70g, 96w%, 0.10mol) in MTBE (750mL) is added aqueous citric acid (500mL 0.25M). The mixture is stirred until all solids were dissolved. The pH of the aqueous layer is about 3 to 5. The layers are then separated, and the organic layer is sequentially washed with 0.13M aqueous citric acid, water and brine. The organic layer is concentrated under reduced pressure of about 200mmHg at 30°C bath and flushed with 400mL of methanol. The residue is diluted with methanol and submitted to the hydrogenolysis (5.64g 10% Pd/C, 40psi,

40°C, 3 hours). The completion of the reaction is confirmed by HPLC. The reaction mixture is then diluted with 700mL of THF to dissolve the product and then filtered through a Solka-Floc pad to remove the Pd catalyst. The pad is rinsed with 500mL of 2:1 THF:MeOH mixture. The filtrate is concentrated and then flushed with methanol. The residue is diluted with 500mL of methanol and the slurry is stirred at 40°C for 0.5 hour and then aged at room temperature overnight. The product is collected by filtration and the filter cake is washed with methanol. It is dried by sucking air through it until a constant weight is achieved to afford the final product as a white solid (95.3% yield, >98A%).

HPLC conditions: Zorbax SB-C8 4.6 x 250mm; MeCN 10-70% in 15 min; 1.50mL/min, 0.1% $H_3PO_4$; 30°C, UV detection at 220nm. Retention times (min): benzylamine salt **20** (13.7) and the final compound **21** (9.8).